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Severe pulmonary hypertension in advanced aortic valve disease

BANDITA BASU, GEORGE CHERIAN, S. KRISHNASWAMI, I. P. SUKUMAR, AND STANLEY JOHN

From the Department of Cardiology and Cardiovascular Surgery, Christian Medical College Hospital, Vellore, India

SUMMARY Review of haemodynamic data of 151 cases with isolated aortic valve disease revealed severe pulmonary hypertension (pulmonary arterial systolic pressure of 60 mmHg or more) in 17 (11%). The left ventricular end-diastolic pressure was high in all but one case, suggesting that the severe pulmonary hypertension was a reflection of the late stages of aortic valve disease. The majority (64·7%) had a low cardiac index. Premature closure of the mitral valve was seen in 12 of the 17 patients. While the incidence of premature mitral closure was the same as in others with mild and moderate pulmonary hypertension, the average reversed ventriculoatrial gradient was higher in the latter groups.

Severe pulmonary arterial hypertension is considered uncommon in patients with aortic stenosis (Gorlin *et al.*, 1955; Gould *et al.*, 1973). In chronic aortic regurgitation, Goldschlager *et al.* (1973) found right heart failure in only 3 out of 126 cases.

The real incidence of pulmonary hypertension in isolated aortic valve disease has not been well documented and there are only a few reports dealing with selected groups of patients (Braunwald *et al.*, 1963; Lee *et al.*, 1970, 1971). This study in patients with isolated aortic valve disease was undertaken to establish the incidence of severe pulmonary hypertension and to examine the clinical and haemodynamic features of patients in whom it is present.

Subjects and methods

Out of 151 consecutive cases of isolated aortic valve disease who underwent cardiac catheterisation in our laboratory, 43 had a pulmonary arterial systolic pressure of 30 mmHg or more and a mean pressure more than 20 mmHg. The pulmonary arterial systolic pressure was 60 mmHg or more in 17 of these 43 cases; these constitute the group with severe pulmonary hypertension. The male:female ratio was 16:1. Ages ranged from 18 to 55 years with an average of 36·3 years. In addition to routine studies, each case had right and left heart catheterisation and selective angiocardiography. Left heart catheterisation was done through a brachial arteriotomy in all but 2 cases. In 1 case the left ventricle was entered by the transseptal route and in another percutaneous left ventricular puncture was necessary. Pressures were recorded with Statham P23 Db transducers and recorded on an Electronics for Medicine DR8 photographic recorder. The cases were divided into 3 groups according to the type of the valve lesion: 9 patients had pure aortic regurgitation, 5 had dominant aortic stenosis, and 3 had dominant aortic stenosis with significant aortic regurgitation. As one case record was misplaced, the clinical features were analysed in 16 of the 17 patients.

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Results

PRESENTING SYMPTOMS

The symptom common to all was exertional dyspnoea, with effort tolerance from grade 2 to grade 4. Eleven patients had paroxysmal nocturnal dyspnoea; 7 had exertional angina and 1 a history of syncope. Twelve of the 16 patients either gave a past history of congestive cardiac failure or presented in heart failure.

PHYSICAL SIGNS

The majority (11 patients) had considerable cardiac enlargement and all had a palpable left ventricular apical impulse. None had a separate left parasternal heave. The first heart sound was quiet in 6 patients with aortic regurgitation. The second heart sound was single in 3 and paradoxically split in 1; the

pulmonary component was accentuated in 5 cases. A third heart sound was heard in 10 cases and a fourth heart sound in 2. An apical mid-diastolic murmur was heard in 9 patients, but only in those with aortic regurgitation.

ELECTROCARDIOGRAM

The electrocardiograms of 15 patients were analysed. All were in sinus rhythm. Six patients (40%) had a normal frontal QRS axis (0 to +90°), and in 5 of these the axis was between 0 and +30°. In 6 cases (40%) the axis was 0 to −30° and in 3 (20%) between −30 and −90°. No patient had right axis deviation. A prolonged PR interval was found in 4 (26·6%). Left atrial enlargement was present in 10 patients (66·6%) while right atrial enlargement was present in only 1. None had electrocardiographic evidence of right ventricular hypertrophy. All had left ventricular hypertrophy while 3 had complete left bundle-branch block. An infarct pattern was seen in 2 cases (13%) of aortic regurgitation.

CHEST X-RAY FILM

In only 2 patients was there enlargement of the main pulmonary artery and its pulmonary branches. In 40 per cent, there was slight to moderate left atrial enlargement. Pulmonary venous congestion was seen in all.

HAEMODYNAMIC DATA

The Table summarises the haemodynamic data in all 17 patients. The majority (64·7%) had a low cardiac index (below 2·4 l/min per m^2) and a wide arteriovenous oxygen difference. The mean pulmonary arterial pressure was more than 40 mmHg in all. The pulmonary arteriolar resistance was 5 units × m^2 or more in all but 1 patient. Though the cardiac index and pulmonary arterial systolic pressure did not show a linear relation, the patients with higher pulmonary arterial pressures had a lower cardiac index. Of 17 cases, 8 had a raised right ventricular end-diastolic pressure (more than 8 mmHg). All but 1 had a very high left ventricular end-diastolic pressure and pulmonary artery wedge pressure, but there was no linear relation between left ventricular end-diastolic pressure and pulmonary arterial systolic pressure. Simultaneous left ventricular and pulmonary artery wedge pressure recordings in 10 patients showed a reversal of the atrioventricular gradient in 8 and this was seen in another 4 in immediately consecutive recordings. Thus, in 12 out of 17 cases there was haemodynamic evidence of premature closure of the mitral valve. Premature closure of the mitral valve occurred in all the three groups, pure aortic regurgitation, dominant aortic stenosis, and mixed aortic valve disease. Patients with premature closure of the mitral valve had a slightly lower cardiac index (average 2·12 l/min per m^2) compared with those without it (average 2·47 l/min per m^2).

CINEANGIOGRAPHY

Left ventriculography revealed poor contractility in all, with a reduced ejection fraction in those in whom it could be calculated. Two patients showed diastolic mitral regurgitation.

Table *Cardiac catheterisation data*

No.	*Diagnosis*	*PA (mmHg)*	*LVEDP (mmHg)*	*PW (mean) (mmHg)*	*CI (l/min per m^2)*	*AV O_2 (vol%)*	*PMC*	*PAR (units × m^2)*
1	AR	60/30 (40)	20-40	36	1·04	7·3	No*	2
2	AR	60/35 (45)	20-25	22	3·8	4·8	No*	11·9
3	AR	76/36 (50)	50	36	2·9	4·0	Yes*	5
4	AR	80/40 (50)	12	5	1·7	9·7	Yes*	15
5	AR	70/45 (52)	45	36	2·0	8·6	Yes*	8
6	AR	70/36 (45)	30	28	2·0	8·2	Yes*	8·5
7	AR	105/55 (72)	35-40	40	1·5	8·2	Yes*	21·3
8	AR	60/35 (43)	55	25	2·4	7·0	Yes	6·8
9	AR	72/12 (50)	36	30	1·9	6·2	Yes	10
10	AS ar	100/38 (58)	30	22	2·0	6·5	Yes	19
11	AS ar	80/35 (50)	36	36	3·6	4·7	No	8
12	AS ar	60/30 (40)	30	23	2·7	5·8	Yes*	6·3
13	AS ar	77 (RV)†	30-50	—	1·3	8·7	—	—
14	AS	60/30 (40)	15-20	28 (LA)	1·45	11·8	Nodal rhythm	8·3
15	AS AR	100/36 (59)	35	29	2·01	6·4	Yes	15
16	AS AR	86/44 (56)	36	19	1·8	6·7	Yes	29
17	AS AR	70/30 (45)	36	28	2·6	5·5	Yes	6·5

PA, pulmonary artery pressure (mmHg); LVEDP, left ventricular end-diastolic pressure (mmHg); PW, pulmonary artery wedge pressure (mean) (mmHg); CI, cardiac index (l/min per m^2); AV O_2, arteriovenous O_2 difference (vol%); PMC, premature mitral valve closure; PAR, pulmonary arteriolar resistance (units × m^2); AR, aortic regurgitation; AS, aortic stenosis; AS AR, aortic stenosis and aortic regurgitation; AS ar, dominant aortic stenosis with mild aortic regurgitation.

* Simultaneous left ventricular and pulmonary artery wedge pressure recording.

† PA not entered.

Discussion

Severe pulmonary hypertension is considered an uncommon haemodynamic finding in patients with isolated aortic valve disease (Gorlin *et al.*, 1955; Gould *et al.*, 1973). The presence of pulmonary hypertension however is likely to be related to the stage of the disease, and to reflect the left ventricular end-diastolic pressure. Braunwald *et al.* (1963) found a pulmonary arterial systolic pressure higher than 30 mmHg in 11 per cent of patients with aortic stenosis, but the number with a pressure over 60 mmHg was not indicated. In the present series, 43 out of 151 (28·4%) patients had a pulmonary arterial systolic pressure over 30 mmHg. Lee *et al.* (1970) reported that 14·7 per cent of 34 patients with aortic stenosis had a pulmonary arterial systolic pressure more than 60 mmHg. In another report they found that 2 of 10 patients with severe aortic regurgitation had a pulmonary arterial systolic pressure more than 60 mmHg (Lee *et al.*, 1971). The present study showed an 11 per cent incidence of severe pulmonary hypertension (more than 60 mmHg pulmonary arterial systolic pressure) in an unselected group of 151 patients with aortic valve disease.

The cardiac index was low in the majority (64·7%) of our patients, and in all but 1 the left ventricular end-diastolic pressure was high. This suggests that the pulmonary hypertension was a manifestation of a late stage of aortic valve disease. It is not surprising that there was no linear relation between the end-diastolic pressure and pulmonary arterial systolic pressure. It is known that once the left atrial mean pressure exceeds 25 mmHg, the increase in pulmonary arterial pressure does not maintain a linear relation with the increase in left atrial pressure. The pulmonary arterial pressure increases more than expected, because of the development of active pulmonary vasoconstriction (Dexter *et al.*, 1950). The pulmonary arteriolar resistance was raised in all but one of our patients.

In the present series, 12 out of 17 cases with severe pulmonary hypertension showed premature closure of the mitral valve with reversed diastolic gradient between 2·6 and 6 mmHg. It is well known that premature closure of the mitral and tricuspid valve occurs in severe aortic regurgitation (Spring *et al.*, 1972). Premature closure of the mitral valve has been thought to protect the pulmonary vascular bed from aortic regurgitant flow and consequent raised pressures (Rees *et al.*, 1964; Spring *et al.*, 1972). To verify this hypothesis, we compared these patients with severe pulmonary hypertension with those with mild and moderate pulmonary hypertension in association with isolated aortic valve disease. Of 151 patients, 19 had mild pulmonary hypertension (pulmonary arterial systolic pressure more than 30 mmHg, but less than 40 mmHg, and mean pulmonary artery pressure more than 20 mmHg) and 7 had moderate pulmonary hypertension (pulmonary artery systolic pressure more than 40 mmHg, but less than 60 mmHg). In the mild pulmonary hypertension group, 12 out of 19 patients had premature mitral closure with reversed ventriculoatrial gradient between 2 and 22 mmHg (average 8·7 mmHg). The patients with moderate pulmonary hypertension showed premature mitral closure in 6 of 7 cases, with reversed gradient between 5·5 and 13 mmHg (average 8·9 mmHg). Thus in the patients with mild and moderate pulmonary hypertension taken together the incidence of premature closure of the mitral valve (70%) was the same as in the group with severe pulmonary hypertension (70%). However, the average reversed gradient was higher in the former group (8·8 mmHg) than in the latter group (4·6 mmHg). The present study shows that premature closure of the mitral valve does not always prevent the development of pulmonary hypertension. However, patients with larger reversed ventriculoatrial gradients had a lower degree of pulmonary hypertension. In this series premature mitral closure occurred in patients with aortic regurgitation, in those with aortic stenosis, and with combined lesions. Mild to moderate diastolic mitral regurgitation has been reported to occur frequently (96% of cases) in aortic regurgitation with premature closure of the mitral valve (Spring *et al.*, 1972). In some patients with aortic regurgitation, the Austin-Flint murmur has been attributed to diastolic mitral regurgitation (Lochaya *et al.*, 1967).

The quiet first heart sound in aortic regurgitation can also be explained by premature closure of the mitral valve (Meadows *et al.*, 1963). The fourth heart sound in aortic regurgitation with a quiet or absent first heart sound may be the premature closure sound of the mitral valve (Wigle and Labrosse, 1965). Spring *et al.* (1972) attribute it to forcible atrial contraction against a closed mitral valve.

A prolonged PR interval has been reported to be a frequent finding in cases with aortic regurgitation (Herbert, 1967). In the present series, 4 cases had a prolonged PR interval. A prolonged PR interval in such a situation ensures early left atrial contraction (relative to ventricular systole), so that its contribution to the forward flow is not affected by premature closure of the mitral valve (Herbert, 1967).

In patients with isolated aortic valve disease, the clinical examination more often provides a clue to the presence of pulmonary hypertension, than does

radiological examination or the electrocardiogram. While a palpable right ventricular heave was not found, in 5 cases the pulmonary component of the second sound was accentuated. The electrocardiogram analysis showed neither right axis deviation nor right ventricular hypertrophy (by voltage criteria) in any patient. Wood (1958) analysed 250 cases of aortic stenosis and observed that the electrocardiogram was normal in trivial and most moderate cases. In severe cases, left ventricular preponderance with secondary T wave inversion was found in 80 per cent, and left bundle-branch block in 14 per cent of patients. Mitchell *et al.* (1954) reviewed 88 cases of pure aortic stenosis and found that in 84 per cent there was electrocardiographic evidence of left ventricular hypertrophy, but in none was there right ventricular hypertrophy. Gould *et al.* (1973) in their single case of aortic stenosis with right heart failure observed right axis deviation.

The pathogenesis of pulmonary hypertension in aortic valve disease appears to be similar to that in mitral valve disease. The raised left atrial pressure, secondary to the raised left ventricular end-diastolic pressure, in the first place leads to a passive increase in pulmonary arterial pressure and later to reactive vasoconstriction. McHenry *et al.* (1974) reported 7 patients with severe aortic stenosis and increased pulmonary arteriolar resistance (more than 7·9 units × m^2), who deteriorated suddenly after catheterisation. Postoperative study in 2 survivors showed that pulmonary vascular resistance had returned to normal, thus confirming that earlier pulmonary hypertension had been the result of reactive vasoconstriction.

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Requests for reprints to Professor George Cherian, Cardiology Department, Christian Medical College Hospital, Vellore 632 004, India.